SMITHSONIAN MISCELLANEOUS COLLECTIONS.

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THE TONER LECTURES

INSTITUTED TO ENCOURAGE THE DISCOVERY OF NEW TRUTHS FOR THE ADVANCEMENT OF MEDICINE.

LECTURE I.

ON THE STRUCTURE OF CANCEROUS TUMORS AND THE MODE IN WHICH ADJACENT PARTS ARE INVADED.

BY

J. J. WOODWARD, ASSISTANT SURGEON, U. S. A.

DELIVERED MARCH 28, 1873.

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As these leetures are intended to inerease and diffuse knowledge, they have been aeeepted for publieation by the Smithsonian Institution in its "Miseellaneous Colleetions."

JOSEPH HENRY,

Secretary Smithsonian Institution.

SMITHSONIAN INSTITUTION.

Washington, November, 1873.

LECTURE I.

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ON THE STRUCTURE OF CANCEROUS TUMORS, AND THE MANNER IN WHICH ADJACENT PARTS ARE INVADED.

By J. J. Woodward, *Assistant Surgeon, U.S.A.*

Gentlemen:—After much hesitation as to a subject suitable for such an occasion as this, I determined to invite your attention to certain considerations with regard to Cancer, a disease which merits study both because of the considerable mortality it produces—more than six thousand deaths annually in the United States*—and because of the obscurity which surrounds every question connected with its origin, its nature, and its successful treatment.

The plan of my discourse is extremely simple. I shall make no attempt to solve this most difficult of all pathological problems. The time has not yet come for any one to tell why cancers originate or how they can be prevented or cured. It is only within the last eight years that we have begun to obtain more definite ideas as to the minute anatomy of these growths, their structural relations to surrounding parts, and the mode in which they multiply in distant organs. The purely anatomical questions involved are still so imperfectly worked out, there is still so much that is unknown, so much that is uncertain, so much as to which we have contradictory testimony from sincere investigators, that a wide field is still open for profitable histological research.

* Census of 1870, deaths of males, 2,301, females, 3,923, total, 6,224.

I propose then, first, to sketch as briefly as possible the modern progress of our knowledge of the minute anatomy of cancerous growths, and to indicate some of the most important points as to which conflicting views still exist; I shall next select a few typical specimens from the microscopical collection of the Army Medical Museum, and endeavor to show, with all modesty, how far the structural details they exhibit correspond with the results obtained by European histologists; where differences are to be noticed I shall not hesitate to point them out, and I hope to be able to present several significant matters of detail which have either been entirely overlooked or not described with the accuracy they deserve.

In illustration of my remarks I shall project upon the screen with an ordinary oxy-calcium lantern some seventy photo-micrographs of the preparations selected for study, by which I hope to render my descriptions more intelligible. The original negatives, most of which I made expressly for this lecture, were taken with various powers from twenty-six to one thousand diameters. The lantern slides, for the sake of sharpness, are reduced to half the number of diameters in each case, and will be projected upon the screen with a magnifying power of fifty diameters.

At the very outset I must bespeak your patience, for though I shall only attempt to touch upon the salient points of my theme, and shall always endeavor to be as brief as is consistent with clearness, I fear I shall detain you beyond the usual period of time allotted to a scientific lecture.

My friend, Dr. Toner, the founder of these lectures, on learning the subject I had selected, expressed the hope that I might be able to contribute something which would aid the general practitioner in the diagnosis of cancerous from other morbid growths, and he justly remarked that the present uncertain condition of the question of diagnosis greatly facilitated the operations of charlatans by enabling them to report cures of

cancer in almost every instance in which a non-malignant growth is removed by their caustic pastes or plasters.

I fully sympathize with the wish thus expressed, but I warn you at the beginning that you have not much to expect from me in this direction. The best knowledge of those who know most of this matter is not yet ripe enough to deal satisfactorily with the question of prognosis in very many cases, and I take it that the question of prognosis is involved in the sort of diagnosis that the general practitioner wants to make. To this subject I will briefly recur in the sequel. Meanwhile I beg you to put all questions of practical application out of your minds, and join me in considering the subject from the point of view of medical science, rather than from that of medical or surgical art.

I begin then by drawing your attention to some of the more striking features in the general advance of our knowledge of the structure of cancer, and especially since the year 1865, when the publication of the work of Thiersch marks an epoch. The previous history of the subject I will pass over as briefly as possible. Suffice it to remind you that in the earlier days of histological investigation the followers of Schwann supposed cancerous and other tumors to arise by free cell development in a formless blastema exuded from the blood-vessels. The causes of the specific characteristics of individual growths were then naturally sought in the blastemata, and the peculiarities attributed to the blastemata were accounted for by supposing them to depend on special morbid conditions or dyscrasiæ of the blood.

The great name of Rokitanski, at whose hands it found its ripest development and most masterly expression, induced the general acceptance of this hypothesis, and it was long the prevailing doctrine in the schools of Europe and America, in spite of the circumstance that the most eager and searching investigations of the physiological chemists utterly failed to discern

any actual differences in the composition of the blood which might serve for such a foundation as the speculation sorely needed.

Nor was it strange that under the influence of the doctrine of dyscrasiæ, the notion should arise that the specialized blastemata must express their specific natures by giving birth to peculiar elementary forms, or that the histologists of the day, very imperfectly acquainted with the normal structure of the body, and bewildered by the multiplicity of forms they observed in morbid growths, should too hastily have adopted the plausible doctrine of specific cancer cells, which more extended observation speedily rendered quite untenable.

The chief actor in the work of sweeping away these speculative opinions was unquestionably Virchow, to whom modern medical science owes so much in so many diverse directions. Virchow found, as any one may still do, in the connective tissue in the vicinity of cancers and many other morbid growths, little groups and rows of cells which he supposed to have been developed out of the normal connective tissue corpuscles. Similar heaps and rows were to be observed in the connective tissue of inflamed organs. The general doctrine was enunciated that the elements of all pathological new formations had their origin in the multiplication of normal cells, and that the connective tissue corpuscles were the actual point of departure in by far the majority of cases. The young cancer elements were, after all, not anatomically different at first from those of granulation tissue; it was in the monstrous development they subsequently underwent, and the premature retrograde metamorphoses by which they were smitten in the midst of their most luxuriant growth, that the key to the external history of cancer was to be sought. Against the doctrine of a primary cancerous dyscrasia, Virchow protested. The origin of the first growth was always to be looked for in local influences. Former injuries of one kind or another could be affirmed in a

large number of cases to have preceded the development of the disease, and though frequently the patient had lost all recollection of the original harm, yet it was in this direction we ought to look, rather than seek to explain away the real difficulties by invoking the aid of an imaginary cachexia.

Now that the brilliant superstructure of the cellular pathology has been shaken to its very foundation, and so much that Virchow labored to teach scattered to all the winds, we cannot, nevertheless, look upon either the man or his works without admiration and respect. None know better than the very men who led in the revolt against his doctrines, how carefully he built them upon the actual facts, so far as at the time they were in his possession; and in the presentation of the facts his descriptions were so clear and generally so nature-true that his works must long remain a mine of wealth to the sincere student. This is especially the case with his book on tumors,* the crowning monument of his industry and genius—a great work, which he has not yet finished. The last part published appeared in 1867; there still remained only the subject of cancer, but it has never been given to the world. During the time which had elapsed since the work was commenced the way had been paved for a histological revolution. In consequence of the multiplication of original investigators throughout Europe, and of the introduction of improved methods of histological research, new facts were being rapidly accumulated, and very many of them were in discordance with the cellular pathology. Still, after all, it ought not to be forgotten that it was two of Virchow's own assistants who made, in his own pathological laboratory, the brilliant series of discoveries which overthrew the splendid generalizations of their master. I refer of course to Von Recklinghausen and Cohnheim. The paper of Cohnheim on inflammation,† published in Virchow's Archiv in 1867,

* Die Krankhaften Geschwülste. Berlin, 1863-7.
† Ueber Entzündung und Eiterung.

marks an epoch in the progress of our pathological views as important as the appearance of the Cellular Pathology.

Two years before the publication of that paper Professor Carl Thiersch, of Erlangen, published in Leipzig a book on epithelial cancer,* which is the first of the more recent special studies to which I wish to invite your attention. Thiersch investigated particularly cancers of the skin. He cut great numbers of thin sections and used methods of research which are still extensively employed in the investigation of morbid growths. His general conclusion was quite adverse to the doctrine of Virchow that cancers originate by the multiplication of the connective tissue corpuscles. So far from this being the case, in cancers of the skin at least, Thiersch declares that the essence of the morbid process is a cell multiplication in the lower soft layers of the epidermis, and in the epithelium of the glandular appendages of the skin, especially the sebaceous follicles. The result of this cell multiplication is the production of cylindrical processes, composed of epithelial cells, and growing into the adjacent connective tissue which disappears before them, precisely as happens during the development of hair sacs and sebaceous glands in the fœtus.

These cancer cylinders branch continually as they grow and increase at the same time in thickness, so that their actual relations are not easily detected in the older parts of the growth. At the margins, on the other hand, single small slices, such as are usually made for microscopical examination, are apt to display numerous transverse or oblique sections of individual cancer cylinders, which have been erroneously interpreted as outlying independent foci, and supposed to originate from the corpuscles of the connective tissue in which they are embedded. If, on the contrary, large sections are made, and especially if a number of thin sections, taken one after another, are compared together, it is easy to recognize that such outlying foci have

* Der Epithelialkrebs. Leipzig, 1865.

only apparently a separate existence, and that everywhere the cancer cylinders stand in direct anatomical connection either with the principal cancerous growth, or, at its margins, with the sebaceous glands or the rete-malpighii.

It is true that a certain amount of cell multiplication takes place in the connective tissue between the cancer cylinders. It is also true that in many cases the papillæ of the skin elongate, branch, and form a prominent framework for the luxuriant epithelial growth which takes place upon their surface. But these morbid processes in the connective tissue are to be regarded as quite subordinate to the proliferation of the deeper epithelial layers which produces the cancer cylinders; and it must be remarked that while the elements of the cancer cylinders have all the epithelial characteristics which might be expected from their origin, the progeny of the connective tissue corpuscles is a small-celled brood not unlike what is to be observed in ordinary granulation tissue.

Thiersch supported his interpretation of the appearances shown in his sections by an appeal to the history of the development of the embryo. The first significant fact after the primitive segmentation of the ovule is the differentiation of that part of the surface of the sphere which corresponds to the future body of the embryo into three distinct layers, a superior, middle and inferior layer. Now as the history of development shows that the epithelium of the skin and of all its glands is derived by direct growth exclusively from the superior or horny embryonic layer, while the connective tissue is derived exclusively from the middle layer, the idea of the origin of the epithelial elements of skin cancers from connective tissue appears so contrary to the laws of normal development that it ought not to be accepted without the most convincing proof.

Such, in brief outline, were the views of Thiersch. I commend his work to you as a most careful and conscientious study. Whatever may be thought of his doctrine, his book is full of

well observed and accurately recorded facts, and its excellent atlas contains numerous faithful representations of appearances which may readily be observed by those who take the pains to follow his method of preparing sections.

In December, 1867, Professor Waldeyer of Breslau published in Virchow's Archiv * an elaborate essay on the development of carcinoma, in which he endeavored to extend the views of Thiersch to all other forms of cancer. For Waldeyer there are no essential differences between the so-called epithelial and other cancers; all are developed alike by the budding out of cancer cylinders from some normal epithelial structure. The cells of the cancer cylinders have everywhere a more or less pronounced epithelial type, as in fact was pointed out by Virchow as long ago as 1847.†

The particular characteristics presented in any given case are dependent to a great extent on the characters of the peculiar epithelial structure from which the cancer cylinders have originated. For example, in the case of cancer of the female breast, which has so long served as the basis of our general ideas of cancer, the cylinders sprout from the epithelium of the ducts and terminal vesicles of the mammary gland, and bud out into the surrounding connective tissue by a process of growth which is only a pathological repetition of the processes by which the gland was first developed; by which it attains its feminine dimensions at puberty; and by which it acquires its temporary increase at each period of lactation. Coincident with the development and growth of the cancer cylinders, the small-celled brood makes its appearance in the intervening connective tissue, but this is by no means the essential or significant part of the process.

Cancers of the stomach originate in like manner from the glands of the gastric mucous membrane which sprout through

* Virchow's Archiv, Bd. 41, S. 470. Die Entwicklung der Carcinome.

† Virchow's Archiv, Bd. 1, S. 94. Zur Entwicklungsgeschichte des Krebses.

the muscle of the mucous membrane into the submucous connective tissue, and thence burrow through the external muscular layers. Similar views are expressed for cancers of the uterus, the ovaries and other organs, while the general description of cancer of the skin, as given by Thiersch, is fully endorsed.

Waldeyer, like Virchow, pronounces against the doctrine of a primary cancer dyscrasia, which he regards as an utterly unjustifiable assumption, and he explains the multiplication of cancerous growths in the internal organs by the transportation of cancerous emboli—actual, detached fragments of living cancer cylinders—through the lymphatics or the veins. His paper is illustrated by several careful figures, evidently drawn from nature. The author was probably not acquainted with Cohnheim's discoveries, published a few months before. Certainly, in his account of the origin of the small-celled brood in the connective tissue between the cancer cylinders, he does not refer to the possibility that a part at least of the new elements might be wandering corpuscles.

In 1869 Dr. Karl Koester published at Würzburg the first part of a work on the development of carcinoma and sarcoma,* which next demands attention. Koester signalizes the fact that when in epithelial cancer of the skin large horizontal sections are prepared, the cancer cylinders are found to anastomose freely, forming a true net-work, which corresponds in form to the normal net-work of the lymphatics. By the action of nitrate of silver on fresh sections he was able to demonstrate the characteristic endothelium of the lymphatics on the surface of the cylinders in many places, while in others he obtained appearances which led him to believe that the cells of the cancer cylinders were produced by the multiplication of these endothelial cells.

The work of Koester, so far as published, was limited to the

*Die Entwicklung der Carcinome und Sarcome, von Dr. Karl Koester. Erste Abtheilung. Würzburg, 1869.

consideration of epithelial cancer of the skin, and alveolar colloid of the stomach, but he suggests the view that other forms of carcinoma and sarcoma have a similar origin. The consideration of these forms was postponed to subsequent parts of his work, which have not yet been published.

The opinion of Koester that the cells of the cancer cylinders are derived from the endothelium of the lymphatics has not been favorably received by the majority of histologists, and I believe pretty much every one who has tried the action of silver in cancer sections after the manner he directs has failed as yet to reproduce the appearances on which this portion of his doctrine is based. That the net-work of cancer cylinders corresponds to the lymphatic passages; that in fact the cylinders, whatever their origin may be, lie in the lymphatics and extend in them, appears to be more generally accepted, and I must avow that it is in strict accordance with all I have been able to observe.

In April, 1870, a paper entitled "A Contribution to the History of the Development of Carcinoma" was published in Virchow's Archiv* by Dr. A. Classen of Rostock. It was based on the study of a case of epithelial cancer of the cornea and sclerotic. It had occurred to the author that the cornea, which had already offered so excellent a field for the study of the inflammatory processes, was also especially suited for the study of the mode in which cancerous growths are developed. He arrived at conclusions very different from those of his predecessors. For him the cells of the cancer cylinders, and indeed all the new elements of cancerous growths, are no other than migrated white blood corpuscles escaped from the blood-vessels after the fashion first pointed out by Cohnheim.

He calls attention to the rich development of blood-vessels around cancerous growths, and to the comparative sluggishness

* Virchow's Archiv, Bd. 50, S. 56. Ueber ein Cancroid der Cornea und Sclera, ein Beitrag zur Entwicklungsgeschichte der Carcinome.

of the circulation in the tortuous veins, which in properly prepared sections are found, as might be expected, to contain great numbers of white corpuscles. The small-celled brood first appears in the connective tissue stroma immediately around the blood-vessels. Between these little lymphoid cells and the large epithelial forms of the cancer cylinders every transition can be observed. When we remember the structure of connective tissue, and the manner in which Von Recklinghausen has shown its little cavities and passages to open into the lymphatic capillaries, we shall not be surprised that it is in these, the nearest available cavities, that the new elements accumulate and develop into the cancer cylinders; for Classen agrees with Koester that the cylinders lie in the lumen of the lymphatics; he differs from him only as to the source of the component cells. As to the assertions of Thiersch and Waldeyer that the cancer cells are essentially epithelial elements, and therefore can only be the progeny of the horny layer of the embryo and of its derivatives, it appears to him a generalization which the facts do not justify. "I fear," he cries, "that in this way we shall attain a cellular mythology before we shall have a cellular pathology."

And here I pause for a moment to say, that in the latter part of the year 1871, my own study of thin sections led me to the conclusion that the migration of the white corpuscles played a great role in the development of cancerous growths, and that, at least in certain cases, the cancer cylinders were formed by the transformation of these corpuscles, which first accumulated in the lymphatic capillaries and the passages leading to them. In April, 1872, in a brief report published by the Surgeon General,* I advocated this view, though not so exclusively as Classen has done, for I could not avoid saying that I was not

* Report to the Surgeon General of the United States Army on the minute anatomy of two cases of cancer. By Assistant Surgeon J. J. Woodward, U. S. A. Washington, D. C., 1872.

prepared to deny "that transformations of the true gland tissue of the parts involved play a certain role in producing the texture of cancerous growths." But just how far the normal elements are atrophied and perish, and how far at times an ill directed formative activity may lead to their monstrous development,—these are matters on which I said that it was difficult at present to form a judgment.

At the time I wrote that report I had not yet read the paper of Classen. I ought to have read it, I know, for the number of the journal containing it had passed through my hands. Still somehow it escaped me, and I did not come upon it till a month or two after the publication of my report. Now that I have carefully studied it I am more than ever impressed with the importance of the part taken by migrating white corpuscles in the genesis of cancerous growths, but I get no help from Classen with regard to the difficulty just indicated. The case he so carefully describes is one of a growth in a non-glandular part, and it leaves unsolved the question of the behavior of the gland lobules when glands are the seat of the morbid growth.

In June, 1872, Professor Waldeyer published in Virchow's Archiv, a second article on the development of carcinoma,* in which, with all the light of recent discovery, and after a careful revision of the whole subject, he nevertheless substantially reaffirms the views of his first paper. He now admits indeed that the elements of the small-celled brood are migrated white corpuscles, and that Koester's view, that the cancer cylinders lie in the lymphatic passages, is very often correct; but he still holds firmly to the doctrine that the cylinders themselves are always outgrowths from some normal epithelial structure with which they yet retain their connection. He supports his opinion by many new and carefully described details, and by a critical review of the modern literature of the subject. His paper is illustrated by a number of careful

* Virchow's Archiv, Bd. 55, S. 67. Die Entwicklung der Carcinome.

figures, evidently drawn after nature, and is in every way worthy of the most thoughtful consideration of the student of cancer.

Such, gentlemen, is an outline of the recent progress of our knowledge of the structure of cancerous growths, and of their relations to the surrounding parts. I have endeavored to seize and present for your consideration the most salient points. In so doing I have been compelled to omit all mention of many worthy investigators. Perhaps you will think I have already dwelt too long on this historical review, but before referring to my own observations I would beg to speak for a moment of the doctrines taught in two excellent German text-books, translations of which have recently been published in this country. I refer to the surgical pathology of Billroth,* and the pathological histology of Rindfleisch.†

Billroth, who has himself contributed no little to the details of our knowledge of morbid growths, adheres in all essential points to the views of Thiersch and Waldeyer; while Rindfleisch entertains opinions more nearly allied to those of Classen. Rindfleisch admits that perhaps, in cancers involving glands, the glandular epithelium may undergo fissiparous multiplication, and so contribute somewhat, though only, as he thinks, to a moderate extent, to the formation of the cancer cylinders. But he thinks that a far larger part is played by migrated white blood corpuscles, which, instead of being transformed into pus or connective tissue as in inflammation, accumulate in the lymphatic passages and are metamorphosed into epithelium-like elements. I commend these instructive and easily accessible works to your consideration, especially that of Rindfleisch; but I warn you that to read them with advantage you must do so by the side of the microscope.

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* General Surgical Pathology and Therapeutics. By Dr. Theodor Billroth. American edition. New York, 1871.

† A Text-book of Pathological Histology. By Dr. Edward Rindfleisch. American edition. Philadelphia, 1872.

Turning now, from this survey of modern investigation into the structure of cancer, to my own observations, I have endeavored to select from the microscopical collection of the Museum a few instructive specimens to serve as the basis of my remarks. I have selected them from various parts of the body, for while all cancerous growths have certain anatomical points in common, which justify us in speaking of cancer as a particular form of disease, the peculiarities of individual growths, both as to structure and history, are largely modified by their seat.

The first group of illustrations I shall present are taken from a case of epithelial cancer of the larynx (No. 889, Medical Section, Army Medical Museum). This is a cauliflower growth which involved the posterior part of the tongue, the epiglottis and the upper part of the larynx. The patient, who was a discharged soldier, sixty-three years of age, had aphonia, pain in the larynx, obstructed respiration, hemorrhage from the growth, and died October 1, 1867, at the post hospital in this city. Thin sections showed that long, branching, vascular papillæ sprouted from the submucous connective tissue, and were clothed with a luxuriant epithelium, which filled the spaces between them, so that except towards the surface the whole formed a solid mass. The papillæ, having branched many times, appeared in profile in some parts of the sections, in other parts they were cut obliquely or transversely, giving rise to rounded or oval forms. Immediately next to the papillæ there was always a single layer of epithelial cells, more or less distinctly columnar in form, beyond which the cells were irregularly polygonal, and larger the more distant they were from the columnar layer.

Wherever adjacent papillæ were so related as to include spaces, the central epithelial cells were flattened, concentrically grouped, and presented striking examples of the so-called "globes epidermiques" or "pearly globules" so common in epithelial cancer.

The larger epithelial cells bore a striking resemblance to the deeper cells of the epithelium of the back part of the tongue. They had large oval nuclei, many of which were biscuit-formed, many contained two nuclei, but nowhere could clear evidence of actual cell multiplication having taken place be obtained.

In the deeper parts of the growth, the epithelial masses invaded the submucous tissue as thick, closely-arranged cell-cylinders. In these the peripheral cells, next to the connective tissue which separated them, were always columnar in character, the central ones polygonal, and in places concentrically grouped as pearly globules. (Six photographs, Nos. 1 to 6, shown and commented upon.)

The second group of illustrations are selected from a case of epithelial cancer of the leg. The patient, who was about forty-seven years of age, had suffered for a long time from a leg ulcer, which at length penetrated so deeply, and produced such destruction of tissue, that the limb was amputated just below the knee in March, 1871. The disease recurred in the cicatrix, and a second amputation, just above the middle of the thigh, was performed in January, 1872, since which the patient has remained apparently well.

Thin sections showed that long, branching and anastomosing cancer cylinders, connected with the cancerous mass, or with the sebaceous glands and rete-malpighii of the adjoining skin, invaded the sub-cutaneous connective tissue. These, in many places, were grotesquely swollen, and contained in their interiors the well-known "pearly globules." On examining the cylinders with high powers, the peripheral layer of cells immediately adjoining the connective tissue was found to resemble very much the cylindrical epithelium which forms the deepest layer of the normal rete-malpighii, except that they were as a rule a little shorter; the cells in the interior of the cylinders resembled those of the more superficial layers of the rete-malpighii, or even the flattened cells of the epidermis. In the

connective tissue between the cancer cylinders there was an abundant infiltration of small cells. (Nine photographs, Nos. 7 to 15, shown.)

In sections taken from some portions of the edges of this growth a very curious appearance was presented. A large meshed net-work in the deeper layer of the corium was continuous more superficially with narrow parallel anastomosing bands, which ran upwards towards the rete-malpighii, and, entering the papillæ of the corium, could be traced almost to their very apices. On one side this net-work was continuous with the margins of the cancerous growth. (Three photographs, Nos. 16 to 18, shown.)

On examining the bands with higher powers, they at first appeared to be composed of small cells held together by more or less fibrous tissue, but almost anywhere I could satisfy myself that the centre of each contained a blood-vessel, which in some places was found to be filled with white corpuscles. Just below the bases of the papillæ of the corium there was an abundant infiltration of small cells which somewhat obscured the net-work, but the bands could be traced through it, and were clearly continuous with the capillary blood-vessels in the centres of the papillæ.

I greatly regret that, having received this specimen in alcohol, it was impossible to confirm the opinion expressed, by a fine injection; but I have no doubt that the form of this remarkable net-work was determined by a luxuriant development of blood-vessels at the edge of the ulcer, and that the innumerable small cells, found in all parts of the bands which composed the net-work, originally white blood corpuscles, were undergoing a transformation which would ultimately have converted the tissue involved into a portion of the cancer.

I call your attention next to two photographs from an epithelial cancer excised from the left forearm of a woman seventy-four years old. Most of the sections made from this

growth are so similar in their microscopical appearances to those obtained from the last, that it might be supposed they were taken from the same specimen. In parts of some of them, however, the terminal and growing extremities of the slender cancer cylinders are so fairly shown, that I have selected a portion of one of the sections for a couple of photographs.

In the place in question the small cells in the connective

Fig. 1.

Section of an epithelial cancer of the arm, showing the terminal buds of the cancer cylinders. From photo-micrograph No. 19. Magnified 116 diameters.

tissue, into which the cylinders are sprouting, are particularly abundant about the terminal buds. The cylinders themselves are very slender, appearing in section as merely a double row of somewhat quadrangular cells. The upper portion of the first photograph represents the rete-malpighii of the skin, so that the space between the upper parts of the cylinders represents, in fact, skin papillæ greatly swollen transversely. I

wish particularly to insist upon the luxuriant small-celled brood about the terminal buds, which is still better shown in the second photograph, in which a higher power has been used. (Two photographs, Nos. 19 and 20, shown.)

I draw my next illustration from a case of epithelial cancer of the lip, excised from a man about forty-five years of age. A smaller growth had been previously destroyed by caustic, but the disease had recurred in the cicatrix, and was removed by the knife in February, 1871.

The general anatomy of the morbid growth was that of an ordinary epithelial cancer, and I shall not go into its details; but some sections, cut at its edge parallel to the anterior surface of the lip and transversely through the hair follicles of the beard, are so instructive that I have made photographs from them.

These sections show that in the progress of the disease the sebaceous glands and the hair follicles are transformed into cancer tissue, but they show also that, for some distance beyond the point to which outgrowths, actually continuous with the cancer, can be traced, an infiltration of small cells, apparently corresponding in its distribution to the course of the blood-vessels, exists in the connective tissue between the hair follicles. It is difficult to resist the conviction that this small-celled infiltration represents the first step in the morbid process, and ultimately contributes its share to the building up of the cancerous mass. (Six photographs, Nos. 21 to 26, shown.)

I exhibit next a view of a section through the mucous membrane of the lip in the immediate vicinity of another epithelial cancer. On one side the preparation shows one of the labial glands in a nearly normal condition; those of the lobules of the next gland which are nearest the cancer are swollen, opaque and fused together; all the lobules of the next gland have undergone the same change; the next two glands are transformed into opaque cell masses in which no trace of the lobules can be discerned. These transformations of the gland tissue

are accompanied by an abundant small-celled infiltration of the surrounding connective tissue, the luxuriance of which keeps pace with the degree to which the glands are altered. (One photograph, No. 27, shown.)

I trust the foregoing illustrations will enable you to follow me when I say that in epithelial cancers we have to do, on the one hand, with the ingrowing from previously existing epithelial structures of branching epithelial cylinders; on the other hand, with a small-celled infiltration of the connective tissue, the cells of which in all probability have migrated from the blood-vessels. All that I have been able to see inclines me to give my assent to the opinion that the cylinders lie in the lymphatic capillaries, or in distended lymph spaces; the small cells occupy the smaller lymph spaces of the connective tissue in which they are found. The preponderance of the fully formed cancer cylinders, or of the small-celled brood, determines considerable diversity in the details of different growths, and this is increased by the circumstance that in some cases the connective tissue papillæ of the part involved grow outward, and branch as in the first case I presented to you. I cannot pause here even to sketch the varieties thus produced, but I wish to add that I am not prepared to agree with Billroth that Thiersch and Waldeyer were right in regarding it as fully established that the cancer cylinders grow by a multiplication of their epithelial elements by division. On the contrary I wish to draw attention not merely to the fact of the swarm of small cells about the terminal buds of the cylinders, but to the additional circumstance that, in almost every section of epithelial cancer in the Museum collection, I find among the epithelial cells numerous unmistakable wandering corpuscles, often fixed by the reagents used, with their processes extended as in the act of migration.

If Biesiadecki* is right in believing that the ordinary growth

*Rindfleisch, *op. cit.*, p. 101.

of epithelial tissues is effected, not by cell multiplication, but by these wandering corpuscles becoming fixed and developing into epithelial cells, we shall readily understand the significance of this circumstance. But be this as it may I cannot doubt that, in many cases at least, besides the continuous epithelial outgrowth, however that may be effected, a portion of the small-celled brood accumulating in the lymphatic passages

Fig. 2.

Two wandering corpuscles among the epithelial cells of an epithelial cancer. From the same preparation as photo-micrograph No. 29. Magnified 600 diameters.

undergoes a transformation into epithelial forms, and thus contributes its share to the growth of the cancer. (Two photographs, Nos. 28 and 29, shown.)

Before passing from this part of the subject I desire to call your attention to a couple of photographs taken from an epithelial cancer of the lip, which illustrate the manner in which such growths, when they penetrate deeply, invade the voluntary muscles. In such cases, if the section is taken transversely to the

course of the muscular fibres, the first change observed is a small-celled infiltration between the fibres, which remain quite intact, and this accumulation progresses, pushing the fibres more and more apart. (Two photographs, Nos. 30 and 31, shown.)

This condition is not peculiar to the muscles in the neighborhood of skin cancers. I have observed it in the neighborhood of cancers of the mammary gland, and of many other

Fig. 3.

Transverse section of muscle near a cancer, showing the small-celled infiltration between the muscular fibres. From photomicrograph No. 30. Magnified 200 diameters.

parts. If the section be made parallel to the course of the muscular fibres the images obtained are not so readily understood. In such sections we not merely see the cell-infiltration between the fibres, but similar cells above and below individual fibres may readily be supposed to be embedded in their substance, as seen in the next photograph, which is taken from the vicinity of a medullary cancer of the parotid gland. (One photograph, No. 32, shown.)

Now I will not affirm that such mistakes account for the opinions of those who believe that a proliferation of the nuclei of the muscular fibres contributes to the cancerous mass; but I point it out as a possible source of error, and must admit that most generally the cell infiltration between the fibres accumulates to such an extent, before the latter undergo any noteworthy alteration, that it is difficult to trace their ultimate fate.

I invite your attention next to a series of illustrations of growths situated in the female breast.

The first group are taken from a tumor of the right breast, weighing over five pounds, which was removed in November, 1870, from the breast of an apparently healthy young woman. (Surgical section, No. 5734.) The tumor had grown rapidly, was freely movable, and there was no retraction of the nipple. Seen quite recently the patient was apparently in good health, and there has been as yet no recurrence.

When received fresh at the Museum the tumor, on section, was pinkish gray, semi-translucent, and yielded an abundant transparent albuminous juice in which but few cellular elements could be detected. On microscopical examination it proved to be made up of nearly normal gland-ducts and gland-vesicles pushed well apart by a luxuriantly developed connective tissue stroma, through which numerous small cells were scattered. (Four photographs, Nos. 33 to 36, shown.)

Such growths have been called adenoma by some, sarcoma by others, and have been ranked among non-malignant tumors. Sometimes they affect a small portion of the gland only, at other times the greater part, or the whole. With the former group of cases I have had little personal experience; as to the latter, I well remember a case quite similar to this, though in an older patient, which I described in 1859, in the American Journal of the Medical Sciences,* and supposed, at the time, to be non-malignant. Nevertheless it speedily returned

* Vol. 37, New Series, p. 67.

in the cicatrix and destroyed the patient.* The secondary growths had no doubtful anatomy. Billroth† insists on the importance of an early removal of such growths and points out their proneness to undergo a cancerous transformation if they are permitted to remain, and to recur with cancerous characteristics if they are removed too late; while acknowledging the justice of his observations I am disposed to go even still farther in my appreciation of their relation to ordinary cancers.

I next draw your attention to some views from a case of cancer of the left breast, removed in March, 1871. The patient was about forty-five years old, and the tumor had been growing a little over a year, having first made its appearance shortly after an injury to the breast received by falling against the corner of a table. It had attained about the size of a hen's egg at the time of removal. Eighteen months after the operation the patient was still apparently in good health.

In this case portions of the growth presented the ordinary anatomy of scirrhus of the breast, but other portions were in a condition very similar to that described in the last case, except that many of the gland vesicles were dilated into cysts. In numerous places the same milk-duct led to groups of vesicles apparently belonging to the same lobule, some of which were nearly normal, while others had undergone the cystic transformation. Both normal vesicles and cysts were pushed apart by a luxuriant connective tissue, infiltrated with small cells. (Five photographs, Nos. 37 to 41, shown.)

Such a growth would be called cysto-sarcoma if the whole tumor had the structure represented in these photographs, but a large part of it had the ordinary anatomy of scirrhus, and I call attention to the significance of the association of the two lesions in the same breast.

The transformation of some of the vesicles of the mammary

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* *Loc. cit.*, vol. 39, p. 331.
† *Op. cit.*, p. 606.

gland into cysts is an exceedingly frequent occurrence in cancers of the breast, and I exhibit illustrations taken from two other cases. (Three photographs, Nos. 42 to 44, shown.)

I have spoken of the ordinary anatomy of scirrhus of the breast. This has been so frequently described that it must be familiar to you all. A stroma of connective tissue encloses alveoli or spaces which are stuffed with larger or smaller, more or less irregular cells. I wish particularly, however, to insist upon the point that these alveoli are not blind cavities, but communicate with each other so as to form a net-work. The net-work is best seen as such at the peripheral portions of the growth, but it can frequently be made out with more or less distinctness in all parts. The cells which compose it are often deficient in the distinct cell-wall which we recognize in many parts at least of epithelial cancers; they are rather to be described as little masses of protoplasm, with nuclei embedded, and the branching cylinders which we found no difficulty in describing as cell-cylinders in epithelial cancer, are here, very often at least, best described as "nucleated cylinders."

Two cancerous tumors of the breast, made up almost wholly of a net-work of such nucleated cylinders lying in an abundant stroma of connective tissue, were described by me in a report to the Surgeon General, to which I have already referred.* I exhibit a photograph from one of these growths. (One photograph, No. 45, shown.)

The other case mentioned in the report was particularly interesting because after the extirpation of the right breast another tumor formed in the left, and the disease subsequently generalized itself, secondary tumors appearing in the liver, the spleen and the ovaries.

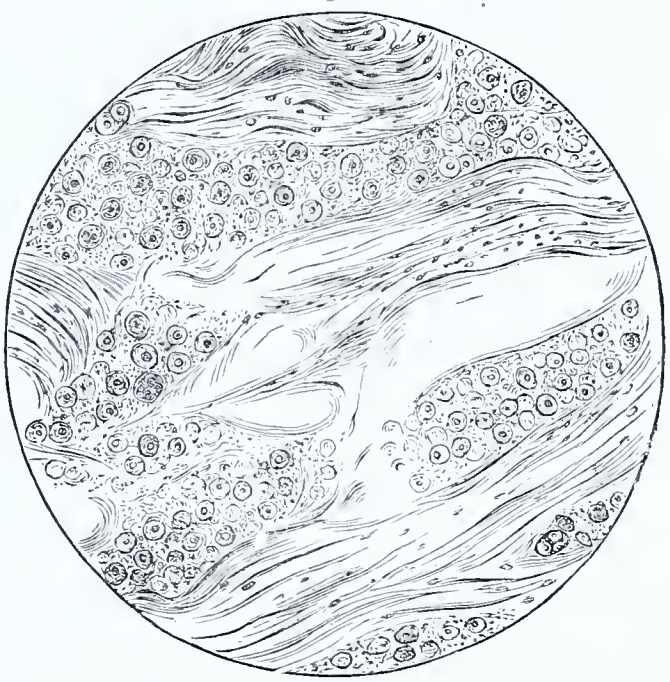
In both the liver and the spleen the secondary tumors were very small; smallest in the liver, in which they varied from the size of a pea to that of a pin's head. They were com-

*See note on page 11, *supra*.

posed of a net-work of nucleated cancer cylinders lying in a connective tissue stroma as shown in the next photograph, which represents one of the nodules in the liver, in which some of the cylinders are cut transversely across. (One photograph, No. 46, shown.)

The ovaries were transformed into oval nodulated scirrhus masses about an inch and three-quarters in long diameter, and

Fig. 4.



Section of mammary cancer, showing branching nucleated cylinders. From the same preparation as photo-micrograph No. 45. Magnified 400 diameters.

these also were composed of similar cylinders embedded in a connective tissue stroma. (One photograph, No. 47, shown.)

I add here two additional representations of the nucleated cylinders in cancers of the breast. The first is taken from a tumor which was extirpated in September, 1869. The woman was forty-three years of age. The disease reappeared in the cicatrix, and was again extirpated in May, 1870. It again recurred in July, 1870, and terminated fatally in June, 1871;

secondary growths were found after death in the stomach and spleen. The case is described in detail in Circular No. 3.* The photograph gives side views of several of the nucleated cylinders, and of the connective tissue between them. (One photograph, No. 48, shown.)

The other photograph is taken from a scirrhus of the breast, extirpated in March, 1871, the subsequent history of which is unknown. (Surgical section, Army Medical Museum, No. 5903.) The cylinders are narrow as compared with those shown in the last picture. (One photograph, No. 49, shown.)

Towards the margins of a growing mammary cancer it is not uncommon for the cylinders to be so slender and so tortuous as to appear in thin sections like small elongated cell groups, such as have been supposed to originate in the proliferation of the connective tissue corpuscles. A comparison of a number of adjacent sections will show their real nature. Two views, taken from one of the breasts described in my report to the Surgeon General, will serve to illustrate this point. (Two photographs, Nos. 50 and 51, shown.)

In the case of cancer of the breast, as we have already seen in epithelial cancers, there may be three explanations of the genesis of the cancer cylinders, so far at least as they are new formations. Either they are outgrowths from the epithelium of the ducts and vesicles of the diseased gland, or they originate by the transformation of the small-celled infiltration, which here, as in skin cancers, is conspicuous in the connective tissue stroma, or both these processes may contribute. A decision between these possibilities is still more difficult than in the case of skin cancers. In attempting the solution of the question it is important to observe the behavior of the gland-ducts and vesicles themselves in growing cancers, and to endeavor to ascertain the transformations they undergo. Some of the photographs shown this evening illustrate at least one of these

* Circular No. 3, Surgeon General's Office, 1871, p. 266.

transformations about which there can be no question, namely, the occasional conversion of the gland vesicles into cysts. But there is another alteration in those of the gland vesicles which are most nearly normal, that can be seen in the sections from which these photographs were taken, and that has been shown in one or two of the photographs; namely, an increased number of epithelial cells in the interior of the vesicles, so that they form several layers, instead of one, which is all that exists in the normal vesicle.* I am inclined to believe that this increase of the number of the epithelial elements may go on until the vesicles and ducts are so distended by them as to form in fact a portion of the cancer cylinders. Whether the increase is due to cell multiplication or to the interpellation of wandering white corpuscles must remain for the present an open question; at all events I find it impossible to admit that the majority of the cancer cylinders have originated either in this way or by the outgrowth of buds from those thus formed. On the contrary the study of the marginal portions of growing breast-cancers inclines me more and more to the opinion that the small-celled brood, accumulating in the lymph spaces, is transformed into cancer cylinders. That this takes place even in skin cancers I have endeavored to show, and it appears to me that the process plays even a more important role in cancers of the breast, forming probably the greater part of tumors which have attained any considerable size, and the whole of those which develop as secondary growths after the complete extirpation of the gland for cancerous disease.

A study of the mode in which cancers of the breast invade the adjacent fat is very suggestive in this connection, and I will give a short account of the process as I have observed it. The outgrowth takes place in two ways — on the one hand the process involves the fat immediately adjoining the carcinoma-

*Stricker's Manual of Histology. American edition, p. 577.

tous mass; on the other hand a small-celled infiltration extends much farther from the main group along the course of the blood-vessels.

In the first instance an infiltration of small cells makes its appearance between the fat cells, accompanied by an increase in the quantity of the matrix by which they are held together. The structural conditions to be observed are precisely the same as may be seen in ordinary inflammation of adipose tissue. In a report on the pleuro-pneumonia of cattle made in June, 1870, and subsequently published by the Commissioner of Agriculture,* I described some sections of the inflamed adipose tissue about the pericardium, taken from a case of that disease in which the appearances were precisely what I have just described, and the photo-micrograph which accompanied the report, but for the somewhat greater size of the fat cells represented, might be supposed to have been taken from the vicinity of a cancerous breast. It is not in its beginning, but in the subsequent history of the small-celled infiltration between the fat cells in cancer, that it differs from the similar small-celled infiltration in inflammation. There is no difficulty in making out this subsequent history in many of the sections belonging to the Museum. The small cells infiltrated between the fat cells increase in number and size, the fat cells themselves are pushed more and more apart, are more and more encroached upon by the morbid growth, and finally disappear without seeming to have contributed anything to the new formation which has replaced them.

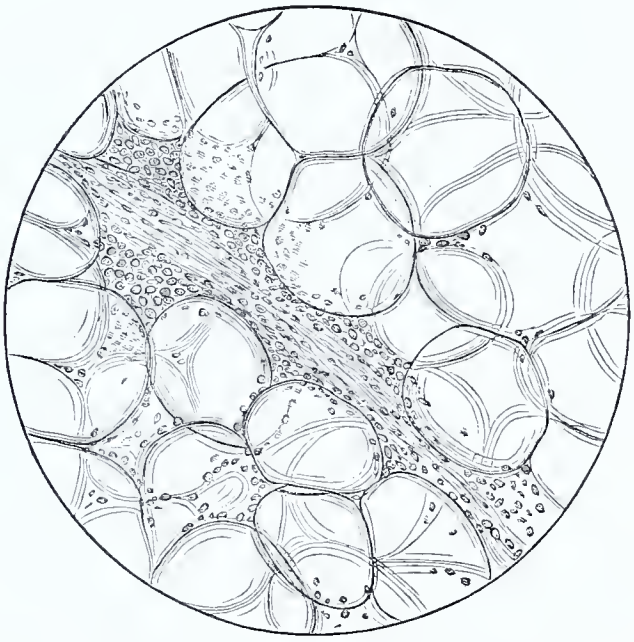
Where the small-celled infiltration has extended from the growth, in the course of the blood-vessels, it appears to occupy primarily the walls of the small veins and the spaces between the immediately adjacent fat cells. In these spaces the behavior of the infiltration is identical with what I have just de-

*Report of the Commissioner of Agriculture on the Diseases of Cattle in the United States. Government Printing Office, 1871, p. 64.

scribed. I find in the whole process conclusive proof that the small-celled infiltration between the fat cells is ultimately transformed into a net-work of cancer cylinders. (Seven photographs, Nos. 52 to 58, shown.)

I call attention next to a few illustrations drawn from a couple of cases of cancer of the stomach. We have already seen that Waldeyer derives cancer of the stomach from the tubular glands of the mucous membrane; from the bottoms of

Fig. 5.



Small-celled infiltration in the course of a minute vein and between the fat cells in the neighborhood of a mammary cancer. From photo-micrograph No. 54. Magnified 200 diameters.

these the cancer cylinders sprout, pass through the submucous connective tissue, invade the muscular coat, and having penetrated this, involve the adjacent parts.

Now all that I have seen of these growths leads me to admit that their primary seat is in the mucous membrane and the subjacent connective tissue; but the determination of the precise origin of the cancer cylinders is surrounded by the

same difficulties which we encountered in the case of cancer of the breast.

The first series of illustrations is drawn from a case of cancer of the pylorus, taken from a man aged thirty-eight, who died in Providence Hospital, in March, 1871. (Medical Section, Army Medical Museum, No. 1079.) The growth assumed the form of a moderate carcinomatous thickening of the walls of the stomach for several inches around the pyloric orifice; the inner surface of the diseased part presenting a superficial area of ulceration near the pylorus, while on the exterior an irregular mass, about an inch in diameter, invaded the gastro-hepatic omentum.

Sections taken from the marginal portions of this carcinomatous thickening showed numerous branching and anastomosing cancer cylinders in the submucous connective tissue, which, between the cylinders, was infiltrated with numerous small cells, the infiltration being most luxuriant just below the mucous membrane. These cylinders in the submucous tissue were continuous with other larger ones in the muscular coat and the submucous adipose tissue. In all of them the peripheral cells were columnar in character, and bore a coarse resemblance to the columnar epithelium of the tubular glands of the stomach; but within these columnar cells, the cylinders were completely filled with polygonal irregular cells, and none of them, as I thought, had any interior free space or lumen; simply as the cells of the interior were not very firmly interadherent they readily fell out of their places from the larger cylinders when thin sections were made, and thus the appearance of tubes lined by an epithelium was simulated. I cannot but note also that the general form and arrangement of the cylinders in the muscular coat, at least, were strikingly similar to what injections teach us of the mode in which the lymphatic network is distributed in this region. (Six photographs, Nos. 59 to 64, shown.)

I add a couple of illustrations from a larger and more luxuriant growth of the same region. The patient was a man aged forty-three, who died in Providence Hospital, in April, 1871, after an illness of about two years. (See Medical Section, Army Medical Museum, No. 1091.) At first the symptoms were those of indigestion, then obstinate vomiting set in, finally a tumor could be felt in the epigastric region, the disease was recognized, and ran its usual course.

The pyloric half of the stomach was involved in the morbid growth, which presented itself as an irregularly lobulated thickening and induration of the coats, in places an inch in thickness. The stomach was adherent to the liver, into the substance of which the carcinomatous infiltration extended, and between the two the mass had softened, forming an abscess-like cavity which communicated with the interior of the stomach by an ulcerated opening through which the fluid contents of the cavity had escaped. The pyloric orifice itself was not much thickened.

Now the structure of the thickened stomach in this case was almost precisely like that of the last, except that the cylinders were as a rule larger, and that there was an abundant small-celled infiltration between the fibre-cells of the muscular coat. (Two photographs, Nos. 65 and 66, shown.)

These two growths represent, so far as I am at present informed, the most common type of cancer of the stomach, and if you picture in your minds the condition which would result if fluid should accumulate in some of the cylinders of such a growth, distending them into cyst-like forms, you would have a correct idea of a somewhat rarer form of cancer of the stomach described in the books, of which, however, we have as yet no example in the microscopical collection of the Museum.

The last case to which I shall call your attention is one of primary cancer of the ovary which illustrates this very point of cystic development. The patient was supposed to be suf-

fering from an ovarian cyst, the removal of which was attempted in October, 1871. (Surgical Section, Army Medical Museum, No. 5944.) On opening the abdominal cavity a medullary cancer of the ovary, of brain-like consistency, was discovered and partially removed. The patient died shortly after.

Sections showed the growth to be made up of a net-work of large cancer cylinders held together by a comparatively scanty connective tissue; many of them were dilated at intervals so as to resemble irregularly oval cysts. They were lined by a layer of polygonal cells which might be compared to an epithelium, and their cavities were filled with an albuminous fluid from which the action of the alcohol used to harden the preparation condensed spherical, somewhat yellowish, semi-transparent bodies of obscure nature. (Three photographs, Nos. 67 to 69, shown.)

Now if in such a growth as this the cystic dilatations, and the epithelium-like lining of the cancer cylinders suggest the idea that they might be transformed Graafian follicles, I must remind you of the other ovarian cancer of which I have already shown you a representation, in which the small size of the nucleated cylinders and the absence of any lumen would seem to exclude such a possibility.

I feel that I should be trespassing upon your patience if I were to continue to multiply individual examples, but I ought not to forget to remind you that the cells of the cancer cylinders may undergo the most varied transformations and degenerations, which aid in making up the complex picture presented by cancerous growths as they actually occur. The cells may increase in size till often, in mammary cancer for example, they rival the larger forms which occur in cancers of the skin. It is from portions of such tumors, in which the cells of the cancer cylinders have grown, till on section the cylinders appear like irregular alveoli of variable size filled with large ir-

regular cells with large nuclei, that the older descriptions of scirrhus and medullary cancer, so familiar to you all, were drawn, and I wish you to remember that these descriptions were true to nature so far as they went. Simply you must understand that growths are none the less cancerous which are extirpated before this later stage has set in. My last illustrations represent sections of the interior portion of a medullary cancer, and some cells scraped from the surface of a well advanced scirrhus, which may serve as samples of the large cell forms referred to, which are in fact what the older writers described as cancer cells. (Five photographs, Nos. 70 to 74, shown.)

If now I recur, as I promised to do, to the question of diagnosis, I think you will understand, without any detailed repetition of the descriptions I have given, that in the present state of our knowledge, we ought, on anatomical grounds, to call any growth a cancer, at the margins of which we find the nucleated or cell cylinders I have described, associated with the infiltration of small cells in the intervening connective tissue. It is not necessary to wait till the cells of the cylinders have acquired any great size in order to arrive at an opinion. It is necessary, however, to cut sections of considerable dimensions, and to prepare them suitably for satisfactory microscopical study; and this requires of course a reasonable amount of practice, while the profitable study of the sections, when prepared, presupposes a practical acquaintance with modern normal and pathological histology.

And at this point the important question of prognosis thrusts itself again upon our attention. Can we be sure that a growth which has the anatomy of cancer will have the history that is usually indicated by the word malignant; that it will ulcerate if left to itself; that it will recur if extirpated; that in either case similar growths will develop in some of the internal organs; and that the patient will surely die from this cause, if not

from the primary disease? On the other hand if a tumor be extirpated which does not possess the anatomy of cancer; in which no proper cancer cylinders have been formed; as for example in the first case of mammary tumor to which I alluded this evening, can we be sure that the growth would not have ultimately acquired the cancerous anatomy if it had been let alone? Can we be sure that it will not, in spite of its timely extirpation, recur and prove fatal?

A proper discussion of these important questions, based upon a consideration of all the evidence, would require much time and thought and be a work of no small labor and difficulty. Of course it cannot be undertaken in the present lecture. Nevertheless it may not be amiss to state that the general tenor of surgical experience would seem to give a negative answer to both these important questions. With regard to the first, the negative answer is the justification of the operation of extirpation, still so generally resorted to, and the motive for urging operative interference as early as possible. It implies a more or less confident belief in the local significance of the primary lesion, and it is not inconsistent with the circumstance that practically the majority of tumors, which on extirpation prove to have the anatomy of cancer, do in fact recur, for the incomplete extirpation of marginal portions of the primary growth, or the existence already at the time of the operation of small secondary growths in distant organs, will sufficiently account for this result, without any more violent supposition.

On the other hand the negative answer to the second question might have been anticipated on purely anatomical grounds, since it would seem that in every cancer there must be a period when the small-celled infiltration of the connective tissue, and perhaps some increase in the number of the epithelial elements of any glandular part involved, is all that has taken place, and whenever this process commences simultane-

ously in a comparatively large area instead of in a small one — in the whole mammary gland for example instead of in a small part of it — the size of a tumor may lead to its extirpation before its anatomy has become characteristic.

But a further consideration of these interesting and important questions would be foreign to my present purpose. I have only wished to-night to present the subject from the anatomical point of view, and if after what I have said you are left with the impression that even our anatomical knowledge of the subject is still far from complete, you will the more readily agree with me when I express the opinion that so far from this branch of the inquiry having been exhausted, additional investigations are urgently needed and ought by all means to be encouraged.

As for the more ambitious efforts to combine together the anatomical facts and the clinical phenomena, so far as either are known, and to frame a comprehensive theory which shall embrace the whole, we must for the present regard them as somewhat premature; but it is a hopeful sign that even in such speculations the mythical notions of specific dyserasiæ and heterologous new formations are being dropped more and more out of sight, and that we are learning more and more to endeavor to explain even the most aberrant phenomena of such a disease as cancer by the ordinary normal laws of development and growth.

LIST OF PHOTO-MICROGRAPHS

EXHIBITED DURING THE LECTURE.

No. 1. Section of epithelial cancer of larnyx. (From No. 2277 Microscopical Section, Army Medical Museum.) Magnified 35 diameters.

No. 2. Same preparation as No. 1, showing a papilla cut across. 200 diameters.

No. 3. Same preparation as No. 1, showing a papilla cut lengthwise, 200 diameters.

No. 4. Same preparation as No. 1, showing a small "globule epidermique." 200 diameters.

No. 5. Same preparation as No. 1, showing a large "globule epidermique." 200 diameters.

No. 6. Same preparation as No. 1, showing two cancer cylinders. 200 diameters.

No. 7. Section of epithelial cancer of leg (No. 4700 Mic. Sec.), showing narrow cancer cylinders and "globules epidermiques." 35 diameters.

No. 8. Same preparation as No. 7, showing cancer cylinders and diseased sebaceous glands. 35 diameters.

No. 9. Same preparation as No. 7, showing cancer cylinders and "globules epidermiques" connected with a sebaceous gland. 35 diameters.

No. 10. Another photograph from the same tumor as Nos. 7, 8 and 9 (No. 4650 Mic. Sec.), showing "globules epidermiques." 35 diameters.

No. 11. Same preparation as No. 7, showing "globules epidermiques," from the centres of some of which the globules have dropped out. 35 diameters.

No. 12. Same preparation as No. 7, showing narrow cancer cylinders. 200 diameters.

No. 13. Same preparation as No. 7, showing a "globule epidermique." 200 diameters.

No. 14. Same preparation as No. 7, showing the terminations of cancer cylinders. 200 diameters.

No. 15. A view somewhat similar to No. 14, from another section of the same tumor (No. 4646 Mic. Sec.). 200 diameters.

No. 16. Another section of the same tumor as Nos. 7 to 15, showing a net-work of bands on the margin of the cancer (No. 4655 Mic. Sec.). 13 diameters.

No. 17. The lower portion of the view given in No. 16. 35 diameters.

No. 18. The upper portion of the view given in No. 16. 35 diameters.

No. 19. Section of an epithelial cancer of the arm (No. 5880 Mic. Sec.), showing the terminal buds of the cancer cylinders. 110 diameters.

No. 20. A portion of the view given in No. 19. 200 diameters.

No. 21. Section of an epithelial cancer of the lip (No. 3713 Mic. Sec.), showing small-celled infiltration between the hair follicles beyond the margins of the cancer. 13 diameters.

No. 22. Another similar section from the same tumor as No. 21 (No. 3713 Mic. Sec.). 13 diameters.

No. 23. Another view of the same preparation as No. 22, showing the relation of the small-celled infiltration to the sebaceous glands. 35 diameters.

No. 24. Another view of the same preparation as No. 21, showing the relation of the small-celled infiltration to the hair follicles. 35 diameters.

No. 25. Another view from the same case as Nos. 21 to 24 (No. 3726 Mic. Sec.), showing the small-celled infiltration around a hair follicle. 110 diameters.

No. 26. A similar view to No. 25, from another part of the same preparation. 110 diameters.

No. 27. Epithelial cancer of the lip (No. 4750 Mic. Sec.), slice near the edge of the tumor, showing diseased labial glands. 13 diameters.

No. 28. Wandering corpuscles among epithelial cells in an epithelial cancer (No. 5881 Mic. Sec.). 500 diameters.

No. 29. A similar view from the same preparation as No. 28. 500 diameters.

No. 30. Invasion of muscle by cancer, transverse section (No. 5862 Mic. Sec.). 200 diameters.

No. 31. Another view of the same preparation as No. 30. 200 diameters.

No. 32. Invasion of muscle by cancer, longitudinal section (No. 3692 Mic. Sec.). 200 diameters.

No. 33. Tumor of the female breast (No. 3852 Mic. Sec.). Gland ducts and vesicles pushed apart by a stroma of connective tissue. 35 diameters.

No. 34. Another view of the same preparation as No. 33. 35 diameters.

No. 35. A portion of the view given by No. 33. 110 diameters.

No. 36. A portion of another section of the same tumor as No. 33 (No. 3851 Mic. Sec.), showing the connective tissue stroma, etc., with a higher power. 200 diameters.

No. 37. Cysto-carcinoma of the female breast (No. 5613 Mic. Sec.). 35 diameters.

No. 38. Another part of the same section as No. 37. 35 diameters.

No. 39. Portion of same view as No. 38. 110 diameters.
No. 40. Portion of same view as No. 39. 200 diameters.
No. 41. Portion of same view as No. 37. 200 diameters.
No. 42. Cancer of breast with cysts (No. 4023 Mic. Sec.). 35 diameters.
No. 43. Cancer of breast with cysts (No. 2398 Mic. Sec.). 35 diameters.
No. 44. Another view from the same case as No. 43 (No. 3373 Mic. Sec.). 35 diameters.
No. 45. Cancer of breast (No. 3489 Mic. Sec.), showing branching nucleated cylinders. 200 diameters.
No. 46. Cancer of liver (No. 2393 Mic. Sec.), showing nucleated cylinders cut across. 200 diameters.
No. 47. Cancer of ovary (No. 2452 Mic. Sec.), showing nucleated cylinders cut across. 200 diameters.
No. 48. Cancer of breast (No. 3519 Mic. Sec.), showing side view of nucleated cylinders. 200 diameters.
No. 49. Cancer of breast (No. 4516 Mic. Sec.), showing side view of nucleated cylinders. 200 diameters.
No. 50. Cancer of breast (No. 4631 Mic. Sec.), showing apparent cell multiplication. 200 diameters.
No. 51. Cancer of breast (No. 4630 Mic. Sec.), showing apparent cell multiplication. 200 diameters.
No. 52. Cancer of breast (No. 4512 Mic. Sec.), showing the invasion of the adjacent adipose tissue. 35 diameters.
No. 53. Cancer of breast (No. 4951 Mic. Sec.), showing the invasion of the adjacent adipose tissue. 35 diameters.
No. 54. Portion of the same section as No. 53. 200 diameters.
No. 55. Another portion of the same section as No. 53. 200 diameters.
No. 56. Cancer of the breast (No. 3650 Mic. Sec.), showing the invasion of adipose tissue. 200 diameters.
No. 57. Another portion of the same section as No. 56. 200 diameters.
No. 58. Portion of the same section as No. 52. 200 diameters.
No. 59. Perpendicular section of cancer of stomach (No. 4504 Mic. Sec.). 13 diameters.
No. 60. Portion of the same view as No. 59. 35 diameters.
No. 61. Another section from the same tumor as Nos. 59 and 60 (No. 4508 Mic. Sec.). 13 diameters.
No. 62. Portion of same view as No. 61. 35 diameters.
No. 63. Portion of same view as No. 62. 110 diameters.
No. 64. Portion of same view as No. 63. 200 diameters.
No. 65. Perpendicular section through the muscular coat of a cancerous stomach (No. 4715 Mic. Sec.). 35 diameters.
No. 66. Portion of the same view as No. 65. 110 diameters.
No. 67. Cysto-carcinoma of ovary (No. 4699 Mic. Sec.). 110 diameters.

No. 68. Another view of the same section as No. 67. 110 diameters.
No. 69. Portion of same view as No. 68. 200 diameters.
No. 70. Section of medullary cancer of parotid (No. 5907 Mic. Sec.) 200 diameters.
No. 71. Another view of the same section as No. 70. 200 diameters.
No. 72. Group of so-called cancer cells. 500 diameters.
No. 73. Group of so-called cancer cells. 500 diameters.
No. 74. Group of so-called cancer cells. 500 diameters.